INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

DATA ELEMENTS FOR TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS

Recommended for Adoption

at Step 4 of the ICH Process

on 17 July 1997

by the ICH Steering Committee

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

DATA ELEMENTS FOR TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS

ICH Harmonised Tripartite Guideline

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 17 July 1997, this guideline is recommended for adoption to the three regulatory parties to ICH

TABLE OF CONTENTS

1. INTRODUCTION 1

1.1 Scope of this guideline 1

1.2 Background 1

1.3 Notes on the format of this document 1

1.4 Definition of data elements 2

1.5 Minimum information 2

2. GUIDELINE: CONTENT OF THE DATA ELEMENTS 3

A. Administrative and Identification Information 3

A.1 Identification of the case safety report 3

A.2 Primary source(s) of information 6

A.3 Information on sender and receiver of case safety report 8

B. Information on the case 9

B.1 Patient characteristics 9

B.2 Reaction(s)/event(s) 13

B.3 Results of tests and procedures relevant to the investigation of the patient 15

B.4 Drug(s) information 15

B.5 Narrative case summary and further information 21

3. GLOSSARY 22

ATTACHMENT 1: Unit List 23

ATTACHMENT 2: Route of Administration List 24

DATA ELEMENTS FOR TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS

1. INTRODUCTION

1.1 Scope of this guideline

The objectives of the working group are to standardize the data elements for transmission of individual case safety reports by identifying, and where necessary or advisable, by defining the data elements for the transmission of all types of individual case safety reports, regardless of source and destination. This includes case safety reports for both pre and post approval periods and covers both adverse drug reaction and adverse event reports. It is not intended that this format should be used for cases in the integrated safety summary of a marketing license application dossier. For adverse reactions encountered in clinical trials, this format should be used only for those subject to expedited reporting. The scope of this topic does not encompass the definition of database structures, nor the design of a paper report form, quality control/quality assurance aspects or technical security issues.

1.2 Background

Because of national and international laws, rules, and regulations, individual case safety reports of adverse drug reactions and adverse events need to be transmitted:

- from identified reporting sources to regulatory authorities and pharmaceutical companies;
- between regulatory authorities;
- between pharmaceutical companies and regulatory authorities;
- within authorities or pharmaceutical companies;
- from clinical investigators, via the sponsor, to ethics committees;
- from authorities to the World Health Organization (WHO) Collaborating Center for International Drug Monitoring.

The transmission of such individual case safety reports currently relies on paper-based formats (e.g., yellow cards, CIOMS forms, MedWatch...) or electronic media (e.g. within pharmaceutical companies, or with WHO), usually by on-line access, tape or file transfer.

Considering the large number of potential participants in a world-wide exchange of information, there is a need for an electronic format capable of accommodating direct database to database transmission using message transfers.

Successful electronic transmission of information relies on the definition of common data elements, provided in this document, and standard transmission procedures to be specified by the ICH Electronic Standards for the Transfer of Regulatory Information (ESTRI) Expert Working Group (M2).

This document has taken into account the documents provided by ICH sponsors, the ENS-CARE Single Case Format, EuroSCaPE format, and the CIOMS IA proposal, and comments received following the circulation of these papers.

1.3 Notes on format of this document

Section 2 and its subsections designated A and B contain notes that are directed toward clarifying the nature of the data that should be provided. In addition, there are notes to assist in defining the format that should be used to transmit the data.

In order to distinguish between these notes, the user guidances are presented *in italics* whereas notes for the transmission format are included as SMALL CAPITALS.

If a data element has a limited set of choices, they are presented in ***Bold Italic*** type. The standard, when fully developed, may provide for this information to be transmitted in encoded format.

1.4 Definition of Data Elements

The format for individual case safety reports includes provisions for transmitting all the relevant data elements useful to assess an individual adverse drug reaction or adverse event report. The data elements are sufficiently comprehensive to cover complex reports from most sources, different data sets, and transmission situations or requirements; therefore, not every data element will be available for every transmission. In many, if not most instances, a substantial number of the data elements will not be known and therefore not included in the transmission. Where it was deemed necessary, provisions for unknown/not applicable were included (e.g., outcome, route of administration). However, since the transmission is intended to be electronic, it was thought to be unnecessary to include provisions to assign values of unknown for all data elements. Different ways of including the same data have been provided to cope with differing information contents: e.g., age information can be sent as date of birth and date of reaction/event, age at the time of reaction/event, or patient age group according to the available information (see section B.1.2 and the respective user guidance). In this example, age would be provided by the most precise available data element rather than including multiple elements of redundant data.

Structured data are strongly recommended in electronic transmission and provisions for including information in this way have been made. However, structuring of the data also implies the use of controlled vocabularies, which are not yet available for some data elements. It is anticipated that electronic transmission of individual case safety reports will be implemented without controlled vocabularies until they become available. In certain instances, there are provisions for the transmission of some free text items, including a full text case summary narrative. The transmission of other unstructured data, such as full clinical records or images is outside the scope of this guideline.

1.5 Minimum information

The minimum information for the transmission of a report should include at least one identifiable patient (section B.1), one identifiable reporter (section A.2), one reaction/event (section B.2), and one suspect drug (section B.4). Because it is often difficult to obtain all the information, any one of several data elements is considered sufficient to define an identifiable patient (e.g., initials, age, sex) or an identifiable reporter (e.g., initials, address, qualification). It is also recognized that the patient and the reporter may be the same individual and still fulfill the minimum reporting criteria.

In addition, in order to properly process the report, the following administrative information is needed: The sender identifier (A.3.1.2), the report identification number (s) (A.1.10), and the date of receipt of the most recent information (A.1.7) (see user guidance for A.1.7).

2. GUIDELINE: CONTENT OF THE DATA ELEMENTS

The data elements are divided into sections pertaining to:

A: Administrative and Identification Information

A.1 - Identification of the case safety report

A.2 - Primary source(s) of information

A.3 - Information on sender and receiver of case safety report

B: Information on the Case:

B.1 - Patient characteristics

B.2 - Reaction(s)/event(s)

B.3 - Results of tests and procedures relevant to the investigation of the patient

B.4 - Drug(s) information

B.5 - Narrative case summary and further information

A. ADMINISTRATIVE AND IDENTIFICATION INFORMATION

A.1 IDENTIFICATION OF THE CASE SAFETY REPORT

A.1.1 Identification of the country of the primary source

User Guidance:

Generally, this item would be the only country provided. Provisions are made to include other countries for unusual cases concerning foreign travel and sources of manufactured material (A.1.2 and B.4.k.2.3).

NOTE CONCERNING TRANSMISSION:

THE CODES FOR COUNTRIES ARE DEFINED BY THE TRANSMISSION STANDARD .

A.1.2 Identification of the country where the reaction/event occurred

User Guidance:

For example, if the reaction was detected while the patient was traveling, but the report was made by a health professional on the patient's return.

A.1.3 Date of this transmission

NOTE CONCERNING TRANSMISSION:

FULL PRECISION DATE, I.E., DAY, MONTH, AND YEAR.

A.1.4 Type of report

- ***Spontaneous report***
- ***Report from study***
- ***Other***
- ***Not available to sender (unknown)***

User Guidance:

A separate category for the designation of a literature source is covered in item A.2.2 and is not duplicated in this section which is intended to capture the type of report. If the case in the literature arises from spontaneous observations, type should be ***Spontaneous report****; if the case arises from a study, type should be* ***Report from***

***study**. If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or arise from a study, then this item should be **Other**.*

Differentiation between types of studies, e.g. clinical trials or others is given in section A.2.3.3.

*The **Not available to sender** option allows for the transmission of information by a secondary sender (e.g., regulatory authority) where the initial sender did not specify the type of report; it differs from **Other** which indicates the sender knows the type of report but cannot fit it into the categories provided.*

A.1.5 Seriousness

A.1.5.1. Serious

- ***Yes/no***

A.1.5.2. Seriousness criteria (more than one can be chosen)

- ***Results in death***
- ***Is life-threatening***
- ***Requires inpatient hospitalization or prolongation of existing hospitalization***
- ***Results in persistent or significant disability/incapacity (as per reporter's opinion)***
- ***Is a congenital anomaly/birth defect***
- ***Other medically important condition***

User Guidance:

*The terms **life-threatening** and **other medically important condition** are defined in the ICH E2A guideline. All the criteria apply to the case as a whole and should not be confused with the outcome(s) of individual reactions(s)/event(s) that are provided in section B.2.i.9.*

A.1.6 Date report was first received from source

User Guidance:

For senders dealing with initial information, this should always be the date received from the primary source. When retransmitting information received from another regulatory agency or another company or any other secondary source, receivers should use the date they first received the information.

NOTE CONCERNING TRANSMISSION:

FULL PRECISION DATE, I.E., DAY, MONTH, AND YEAR.

A.1.7 Date of receipt of the most recent information for this report

User Guidance:

Because reports are required to be sent at different times to multiple receivers, the initial/follow up status is dependent upon the receiver. For this reason an item to capture follow-up status is not included. However, the date of receipt of the most recent information taken together with the 'sender identifier' (A.3.1.2) and sender's 'report identification number' (A.1.10) provide a mechanism for each receiver to identify whether the report being transmitted is an initial or follow-up report. For this reason these items are considered necessary for each transmission.

NOTE CONCERNING TRANSMISSION:

FULL PRECISION DATE, I.E., DAY, MONTH, AND YEAR.

A.1.8 Additional available documents held by sender

A.1.8.1 Are additional documents available?

- yes/no

A.1.8.2 List of documents held by sender

User Guidance:

List the documents received from the primary source (e.g., clinical records, hospital records, autopsy reports). It is recognized that these documents may not be obtainable in many instances.

NOTE CONCERNING TRANSMISSION:

FREE TEXT.

A.1.9 Does this case fulfill the local criteria for an expedited report?

- yes/no

User Guidance:

This item is used to provide the sender's local reporting requirements, and the definition of expedited is dependent on the local regulatory requirements. When the countries of origin and destination of the transmission differ, the receiver should be aware that the information may not be applicable to their regulatory requirements.

A.1.10 Report identification number(s)

A.1.10.1 National regulatory authority's case report number

A.1.10.2 Company's case report number

A.1.10.3 Other sender's case report number

User Guidance:

A.1.10.1 and A.1.10.2 are the identifiers given by a national regulatory authority and by a company, respectively. Both identifiers may be transmitted if known. Companies should ensure a single international report number to facilitate the unique identification of a report that may have been sent to many places and subject to multiple retransmissions. A.1.10.3 would be used by senders who are not representing either a pharmaceutical company or a national regulatory authority.

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

A.1.11 Suspected duplicate

- yes

User Guidance:

This item is used when the sender suspects or knows that the report has already been transmitted to the receiver. Only an affirmative answer is needed, otherwise the item is left empty. If known, the suspect duplicate case report number(s) and the other sender(s), where applicable, can be provided.

A.1.11.1 Source(s) of the duplicate (e.g., name of the company, name of regulatory agency)

A.1.11.2 Case report number of the suspected duplicate(s)

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA FOR THE NUMBER AND SOURCE .

A.1.12 Identification number of the report which is linked to this report (repeat as necessary)

User Guidance:

This section is used in the case of e.g. a mother-child pair where both had reactions/events, or of siblings with common exposure, or several reports involving the same patient, or several similar reports from same reporter (cluster). These links do not refer to duplicates, but to links of clinical relevance (the reactions/events are shared among patients or in the same patient and appear pertinent to each other).

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

A.1.13 Report nullification

- ***yes***

User Guidance:

This item is used to indicate that a previously transmitted report should be considered completely void (nullified), for example when the whole case was found to be erroneous. It is essential to use the same case report number previously submitted.

A.1.13.1 Reason for nullification

NOTE CONCERNING TRANSMISSION:

FREE TEXT

A.1.14 Was the case medically confirmed, if not initially from a health professional?

- ***yes/no***

User Guidance:

This section is completed if the primary source of information was a lawyer, consumer, or other non health professional and it is needed because of differences in post marketing surveillance regulations concerning lay reports.

A.2 PRIMARY SOURCE(S) OF INFORMATION

The primary source(s) of the information is a person who reports the facts. This should be distinguished from senders (secondary sources) who are transmitting the information, e.g., industry to regulatory authority.

Any or all of the three subsections (A.2.1, A.2.2., A.2.3) can be used. In the case of a published study or published individual case, the reporter would be the investigator or first author, and details on publication and trial type should also be provided.

A.2.1 Primary source(s) (repeat as necessary)

A.2.1.1 Reporter identifier (name or initials)

User Guidance:

The identification of the reporter may be prohibited by certain national confidentiality laws or directives. The information is only provided when it is in conformance with the confidentiality requirements and this guidance applies to all the subsections of A.2.1. Notwithstanding the above, at least one subsection should be completed to fulfill the general need of having an identifiable reporter. If only the name of the reporter is known and it is prohibited to provide it because of confidentiality requirements, initials can be used.

A.2.1.2 Reporter's address

NOTE CONCERNING TRANSMISSION:

THE FORMAT FOR ADDRESSES ARE DEFINED IN THE TRANSMISSION STANDARD .

A.2.1.3 Country

NOTE CONCERNING TRANSMISSION:

THE CODES FOR COUNTRIES ARE DEFINED BY THE TRANSMISSION STANDARD .

A.2.1.4 Qualification

- ***Physician***
- ***Pharmacist***
- ***Other health professional***
- ***Lawyer***
- ***Consumer or other non health professional***

User Guidance:

In some regions, consumer and lawyer reports are transmitted only when there is medical confirmation.

A.2.2 Literature reference(s)

User Guidance:

References are provided in the Vancouver Convention (known as "Vancouver style") as developed by the International Committee of Medical Journal Editors. The standard format as well as those for special situations can be found in the following reference which is in the Vancouver style. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

A.2.3 Study identification

A.2.3.1 Study name

A.2.3.2 Sponsor study number

User Guidance:

This section would be completed only if the sender is the study sponsor or has been informed of the study number by the sponsor.

A.2.3.3 Study type in which the reaction(s)/event(s) were observed

- ***Clinical trials***
- ***Individual patient use; e.g."compassionate use" or named patient basis***
- ***Other studies***

User Guidance:

Other studies include pharmacoepidemiology, pharmacoeconomics, intensive monitoring, PMS, etc.

A.3 INFORMATION ON SENDER AND RECEIVER OF CASE SAFETY REPORT

A.3.1 Sender

A.3.1.1 Type

- ***Pharmaceutical company***
- ***Regulatory authority***
- ***Health professional***
- ***Regional pharmacovigilance center***
- ***WHO collaborating center for international drug monitoring***
- ***Other (e.g. distributor, study sponsor, or contract research organization)***

User Guidance:

In this context, a pharmaceutical company includes biotechnology companies and other manufacturers required to submit individual case safety reports.

A.3.1.2 Sender identifier

User Guidance:

Identifies the sender, e.g., company name or regulatory authority name. This item should always be completed.

A.3.1.3 Person responsible for sending the report

User Guidance:

Name of person in the company or agency who is responsible for the authorization of report dissemination. This would usually be the same person who signs the covering memo for paper submissions. The inclusion of the name of this person in the transmission may be subject to national or international regulations.

A.3.1.4 Sender's address, fax, telephone and E-mail address

A.3.2 Receiver

User Guidance:

See the User Guidance: concerning the sender (A.3.1).

A.3.2.1 Type

- ***Pharmaceutical company***
- ***Regulatory authority***

- ***Regional pharmacovigilance center***
- ***WHO collaborating center for international drug mo nitoring***
- ***Other (e.g., a company affiliate or a partner)***

A.3.2.2 Receiver identifier (see glossary)

A.3.2.3 Receiver's address, fax, telephone and E-mail address

B. INFORMATION ON THE CASE

B.1 PATIENT CHARACTERISTICS

User Guidance:

In cases where a fetus or suckling infant sustains an adverse reaction/event, information on both the parent and the child/fetus should be provided. Reports of these cases are referred to as parent-child/fetus report. Several general principles are used for filing these reports. If there has been no reaction/event affecting the child/fetus the parent-child/fetus report does not apply. For those cases describing fetal demise or early spontaneous abortion, only a parent report is applicable. If both the parent and the child/fetus sustain adverse events, two reports are provided but they are linked by using sections A.1.12 in each of the reports. When only the child/fetus has an adverse reaction/event (other than early spontaneous abortion/fetal demise) the information provided in this section applies to the child/fetus, and characteristics concerning the parent who was the source of exposure to the drug is provided in section B.1.10.

B.1.1 Patient (name or initials)

User Guidance:

The identification of the patient may be prohibited by certain national confidentiality laws or directives. The information is only provided when it is in conformance with the confidentiality requirements. This also applies to medical record number(s) (B.1.1.1).

B.1.1.1 Patient medical record number(s) and source(s) (if allowable)

User Guidance:

Record numbers may include the GP and/or specialist record(s) number(s), hospital record(s) numbers, or patient/subject identification number in a study.

NOTE CONCERNING TRANSMISSION:
ALPHA/NUMERIC DATA.

B.1.2 Age information

User Guidance:

To be used according to the most precise information available.

B.1.2.1 Date of birth

User Guidance:

If the full date of birth is not known use section B.1.2.2

NOTE CONCERNING TRANSMISSION:
FULL PRECISION DATE, I.E., DAY, MONTH, AND YEAR.

B.1.2.2 Age at time of onset of reaction/event

User Guidance:

If several reactions/events are in the report, use the age at the time of the first reaction/event. For fetal reaction(s)/event(s), use the next item Gestation period when reaction/event was observed (B.1.2.2.1).

When providing the age in decades, please note that, for example, the 7th decade refers to a person in their 60s.

NOTE CONCERNING TRANSMISSION:

THE CODES TO BE USED ARE DEFINED IN THE TRANSMISSION STANDARD BUT SHOULD INCLUDE VARIOUS AGE UNITS (DAYS, WEEKS, MONTHS, YEARS, DECADES).

B.1.2.2.1 Gestation period when reaction/event was observed in the fetus

User Guidance:

The gestation period at the time of exposure is captured in section B.4.k.10.

NOTE CONCERNING TRANSMISSION:

NUMBER AND UNITS (DAYS, WEEKS, MONTHS OR TRIMESTER).

B.1.2.3 Patient age group (as per reporter)

- ***Neonate***
- ***Infant***
- ***Child***
- ***Adolescent***
- ***Adult***
- ***Elderly***

User Guidance:

The terms are not defined in this document and are intended to be used as they were reported by the primary source. This section should be completed only when the age is not provided more specifically in sections B.1.2.2 or B.1.2.3.

B.1.3 Weight (kg)

User Guidance:

The weight at the time of the event/reaction.

NOTE CONCERNING TRANSMISSION:

THE CODES FOR ITEMS B.1.3-B.1.5 ARE DEFINED IN THE TRANSMISSION STANDARD .

B.1.4 Height (cm)

B.1.5 Sex

B.1.6 Last menstrual period date

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATES ARE ACCEPTABLE, I.E., MONTH AND YEAR, OR YEAR ONLY.

B.1.7 Relevant medical history and concurrent conditions (not including reaction/event)

B.1.7.1 Structured information (repeat as necessary)

Disease / surgical procedure / etc.	Start date	Continuing Y/N/U	End date	Comments

User Guidance:

Medical judgment should be exercised in completing this section. Information pertinent to understanding the case is desired such as diseases, conditions such as pregnancy, surgical procedures, psychological trauma, etc. Each of the items in the table can be repeated as necessary. If precise dates are not known and a text description aids in understanding the medical history, or if concise additional information is helpful in showing the relevance of the past medical history, this information can be included in the Comments column.

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATES MAY BE USED FOR BOTH START AND END DATES. THE CONTINUING COLUMN SHOULD ACCEPT VALUES FOR YES, NO AND UNKNOWN, AND THE MAIN DESCRIPTIVE COLUMN WILL HAVE ALPHA DATA IN CONCORDANCE WITH THE CONTROLLED VOCABULARY BEING DEVELOPED.

B.1.7.2 Text for relevant medical history and concurrent conditions (not including reaction/event)

User Guidance:

To be used if structured information is not available in the sender's database. Otherwise, it is preferable to send structured data in segment B.1.7.1.

NOTE CONCERNING TRANSMISSION:

FREE TEXT

B.1.8 Relevant past drug history (repeat the line as necessary)

Name of drug as reported	Start date	End date	Indication	Reactions

User Guidance:

This segment concerns previously taken drugs, but not those taken concomitantly or drugs which may have potentially been involved in the current reaction(s)/event(s). Information concerning concomitant and other suspect drugs is included in section B4. The information provided here may also include previous experience with similar drugs. Medical judgment should be exercised in completing this section. When completing the item concerning the name of the drug it is important to use the words provided by the primary source. Trade name, generic name or class of drug can be used. The term "none" should be used when appropriate, e.g., when there is no previous exposure to the drug or vaccine, or no previous reaction following exposure.

NOTE CONCERNING TRANSMISSION:

THE DATA ELEMENT FOR NAME OF DRUG SHOULD ACCEPT ALPHANUMERIC DATA AND INCLUDE PROVISIONS FOR ACCEPTING THE WORD NONE. THE DATA ELEMENTS FOR REACTIONS AND INDICATIONS WILL CONFORM TO THE CONTROLLED VOCABULARY WHEN FULLY IMPLEMENTED. BOTH DATES MAY BE IMPRECISE.

B.1.9 In case of death

B.1.9.1 Date of death

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATE FORMAT.

B.1.9.2 Reported cause(s) of death (repeat as necessary)

NOTE CONCERNING TRANSMISSION:

CONTROLLED VOCABULARY ARE USED WHEN FULLY IMPLEMENTED.

B.1.9.3 Was autopsy done?

Yes/No/Unknown

B.1.9.4 Autopsy-determined cause(s) of death (repeat as necessary)

NOTE CONCERNING TRANSMISSION:

CONTROLLED VOCABULARY ARE USED WHEN FULLY IMPLEMENTED.

B.1.10 For a parent-child/fetus report, information concerning the parent

User Guidance:

This section is used only in the case of a parent-child/fetus report where the parent had no reaction/event. See User Guidance: for section B.1. Guidance regarding confidentiality is provided in B.1.1, and should be considered before providing the parent identification. For the subsections B.1.10.4 through B.1.10.8 review the guidances provided for B.1.3 through B.1.5 and B.1.7 through B.1.8.

B.1.10.1 Parent identification

B.1.10.2 Parent age information

User Guidance:

Use the date of birth if the precise birthday is known, otherwise use age.

B.1.10.2.1 Date of birth of parent

NOTE CONCERNING TRANSMISSION:

FULL PRECISION DATE.

B.1.10.2.2 Age of parent

B.1.10.3 Last menstrual period date

User Guidance:

If a precise date is not available, complete the gestation period at time of exposure in B.4.k.10.

NOTE CONCERNING TRANSMISSION:
FULL PRECISION DATE.

B.1.10.4 Weight (kg) of parent

B.1.10.5 Height (cm) of parent

B.1.10.6 Sex of parent

B.1.10.7 Relevant medical history and concurrent conditions of parent (not including reaction/event)

B.1.10.7.1 Structured information (parent)

Disease / surgical procedure/ etc.	Start date	continuing Y/N/U	End date	Comments

B.1.10.7.2 Text for relevant medical history and concurrent conditions of parent (not including reaction/event)

B.1.10.8 Relevant past drug history of parent

Name of drug as reported	Start date	End date	Indication	Reactions (if any and known)

B.2 REACTION(S)/EVENT(S)

User Guidance:

The designation of "i" in this section indicates that each item is repeatable and that it carries an appropriate correspondence to the same i in all subsections. A separate block (i) should be used for each reaction/event term. For example, if two reactions are observed, the first reaction would be described in items B.2.1.1 through B.2.1.9, and the other reaction would be described in items B.2.2.1 through B.2.2.9.

B.2.i.1 Reaction/event as reported by the primary source

User Guidance:

The original reporter's words and/or short phrases are used to describe the reaction/event. This should be provided in a language agreed upon by sender and receiver. For international transmissions, English is the generally accepted language.

NOTE CONCERNING TRANSMISSION:
ALPHA/NUMERIC DATA.

B.2.i.2 Reaction/event term

User Guidance:

The term can be a sign, symptom or diagnosis. A controlled vocabulary will be used when available. This also applies to the other items of structured data such as indication, diseases in past medical history, etc.

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

B.2.i.3 Term highlighted by the reporter

- ***yes***

User Guidance:

To be used when the primary source indicated that the reaction/event was a major concern or reason for reporting the case. If the information is not explicitly provided by the initial reporter the item should be left blank. Only affirmative answers are needed.

B.2.i.4 Date of start of reaction/event

B.2.i.5 Date of end of reaction/event

B.2.i.6 Duration of reaction/event

User Guidance:

This section can usually be computed from start/end of reaction/event. However, sometimes, both dates and duration are useful, e.g., for a reaction/event of short duration such as anaphylaxis or arrhythmia.

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATES MAY BE USED AND THE DURATION IS DEFINED BY THE TRANSMISSION STANDARD.

B.2.i.7 Time intervals between suspect drug administration and start of reaction/event

User Guidance:

The major uses of intervals are to cover circumstances where both the dates are known but the interval is very short (e.g., minutes, such as in anaphylaxis), and when only imprecise dates are known but more information concerning the interval is known. Dates if available should always be transmitted in the appropriate fields rather than intervals.

When there is more than one reaction/event and more than one suspect drug there is a matrix of intervals between the exposures and reactions/events. B.2.i.7 captures the interval between each reaction/event and one suspect drug. B.4.k.13 captures the interval between each suspect drug and one reaction/event. The sender should choose the drug and reaction/event considered based on information available and/or the reporter's judgment. The complexity of the intervals highlights the desirability of providing dates.

NOTE CONCERNING TRANSMISSION:

CODES ARE DEFINED IN THE TRANSMISSION STANDARD .

B.2.i.7.1 Time interval between beginning of suspect drug administration and start of reaction/event

B.2.i.7.2 Time interval between last dose and start of reaction/event

B.2.i.8 Outcome of reaction/event at the time of last observation

- ***recovered/resolved***
- ***recovering/resolving***
- ***not recovered/not resolved***
- ***recovered/resolved with sequelae***
- ***fatal***
- ***unknown***

User Guidance:

In case of irreversible congenital anomalies the choice, ***not recovered/not resolved*** *should be used.*

Fatal *should be used when death is possibly related to the reaction/event. Considering the difficulty of deciding between "reaction/event caused death" and "reaction/event contributed significantly to death", both were grouped in a single category. Where the death is unrelated, according to both the reporter and the sender, to the reaction/event,* ***death*** *should not be selected here, but is reported only under section B.1.9.*

B.3 RESULTS OF TESTS AND PROCEDURES RELEVANT TO THE INVESTIGATION OF THE PATIENT

User Guidance:

This section captures the tests and procedures performed to diagnose or confirm the reaction/event, including those tests done to investigate (exclude) a non-drug cause, e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis. Both positive and negative results should be reported. While structured information is preferable, provisions are made to transmit the information as free text in B.3.2.

B.3.1 Structured information (repeat as necessary)

Date	Test	Result	Unit	Normal low range	Normal high range	More information available (Y/N)

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATES MAY BE USED. THE DESCRIPTION OF THE TEST'S, RESULTS, UNITS AND NORMAL RANGES WILL BE IN FREE TEXT UNLESS COVERED BY A CONTROLLED VOCABULARY. THE COLUMN ENTITLED "MORE INFORMATION AVAILABLE" ACCEPTS ONLY YES OR NO.

B.3.2 Results of tests and procedures relevant to the investigation

NOTE CONCERNING TRANSMISSION:

FREE TEXT

B.4 DRUG(S) INFORMATION

User Guidance:

This section covers both suspect drugs and concomitant medications including biologicals. In addition, the section can be used to identify drugs thought to have an interaction. For each drug, the characterization of the drug role (B.4.k.1) is that indicated by the primary reporter, i.e., the original source of the information. The

designation of k in this section indicates that each item is repeatable and that it carries an appropriate correspondence to the same k in all subsections. A separate block (k) should be used for each drug. Drugs used to treat the reaction/event should not be included here.

B.4.k.1 Characterization of drug role

Suspect/Concomitant/Interacting

User Guidance:

Characterization of the drug as provided by primary reporter. By convention, all spontaneous reports have at least one suspect drug.

B.4.k.2 Drug identification

User Guidance:

Drug substance name and/or proprietary medicinal product name is provided as it was reported.

B.4.k.2.1 Proprietary medicinal product name

User Guidance:

The name should be that used by the reporter. It is recognized that a single product may have different proprietary names in different countries, even when produced by a single manufacturer.

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA

B.4.k.2.2 Active substance name(s)

User Guidance:

Provide the INN(s) or drug substance name(s) or drug identification code(s) if no name exists. For combination products, each active ingredient should be specified. This information, as well as that requested in for Proprietary medicinal product name (B.4.k.2.1) may not be known for concomitant or interacting drugs when the sender is a pharmaceutical company. In the case of blinded trials, in the exceptional circumstance when the blind has not been broken, the word "blinded" should precede the names of the drugs included in the study. Placebo can be included as a drug.

B.4.k.2.3 Identification of the country where the drug was obtained

NOTE CONCERNING TRANSMISSION:

THE CODES FOR COUNTRIES ARE DEFINED BY THE TRANSMISSION STANDARD .

B.4.k.3 Batch/lot number

User Guidance:

This information is particularly important for vaccines and biologicals. The section allows for multiple batch/lot numbers, each separated by a delimiter defined by the transmission standard chosen. Provide the most specific information available. For expiration date and other related information, see additional information on drug (B.4.k.19).

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA, THE DELIMITER TO SEPARATE BATCH AND LOT NUMBERS TO BE DEFINED BY THE TRANSMISSION STANDARD .

B.4.k.4 Holder and authorization/application number of drug

User Guidance:

If relevant and known, provide the name of the holder and the authorization number in the country where the drug was obtained when the case report is sent to that country. These items apply to both applications and authorizations. Pharmaceutical companies provide this information for their own suspect drug(s).

B.4.k.4.1 Authorization/Application Number

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

B.4.k.4.2 Country of authorization/application

NOTE CONCERNING TRANSMISSION:

THE CODES FOR COUNTRIES ARE DEFINED BY THE TRANSMISSION STANDARD .

B.4.k.4.3 Name of holder/applicant

NOTE CONCERNING TRANSMISSION:

ALPHA/NUMERIC DATA.

B.4.k.5 Structured Dosage Information

e.g. 2mg three times a day for five days

B.4.k.5.1	**dose (number)**	2
B.4.k.5.2	**dose (unit)**	mg
B.4.k.5.3	**number of separate dosages**	3
B.4.k.5.4	**number of units in the interval**	1
B.4.k.5.5	**definition of the interval unit**	day
B.4.k.5.6	**cumulative dose to first reaction(number)**	30
B.4.k.5.7	**cumulative dose to first reaction (unit)**	mg

User Guidance:

Please note the side by side illustration of how the structured dosage is provided. For the more complex example of 5mg (in one dose) every other day for 30 days, subsections B.4.k.5.1 through B.4.k.5.7 would be 5, mg, 1, 2, day, 75, mg, respectively. In the same way, 50 mg daily for 2 days would be 50, mg, 1, 1, day, 100, mg. For prolonged chronic therapy, the sender should consider the need to complete the cumulative dose sections.

In the case of a parent-child/fetus report, the dosage section applies to the parental dose.

For dosage regimen that involve more than one dosage form and/or changes in dosage, the information is provided in section B.4.k.6 as text. Alternatively, the sender can provide more than one iteration (k) for the same drug. Categories for "dose unit" and for "definition of the interval" are described in attachment 1.

B.4.k.6 Dosage text

User Guidance:

To be used in cases where provision of structured dosage information is not possible.

NOTE CONCERNING TRANSMISSION:

FREE TEXT

B.4.k.7 Pharmaceutical form (Dosage form)

User Guidance:

E.g., tablets, capsules, syrup.

NOTE CONCERNING TRANSMISSION:

FREE TEXT UNTIL A CONTROLLED VOCABULARY IS AVAILABLE .

B.4.k.8 Route of a dministration

User Guidance:

See suggested vocabulary in the route of administration list in attachment 2. For a parent-child/fetus report this indicates the route of administration of a drug given to the child/fetus. This is usually an indirect exposure such as transmammary but can include more usual routes of administration for other drugs given to the child. The parent route of administration is provided in B.4.k.9.

B.4.k.9 Parent route of administration (in case of a parent child/fetus report)

User Guidance:

This section is used only in a parent-child/fetus report and linked parent reports to indicate the route of administration to the parent.

B.4.k.10 Gestation period at time of exposure

User Guidance:

Use the gestational age at the time of the earliest exposure

NOTE CONCERNING TRANSMISSION:

GESTATION PERIOD AT TIME OF EXPOSURE IS EXPRESSED BY PROVIDING BOTH A NUMBER AND DESIGNATION OF UNITS OF DAYS , WEEKS, MONTHS OR TRIMESTER.

B.4.k.11 Indication for use in the case

User Guidance:

The indication as reported.

NOTE CONCERNING TRANSMISSION:

CONTROLLED VOCABULARY TO BE USED WHEN FULLY IMPLEMENTED .

B.4.k.12 Date of start of drug

NOTE CONCERNING TRANSMISSION:

IMPRECISE DATE FORMATS IN THIS SECTION AS WELL AS IN B .4.K.14

B.4.k.13 Time intervals between drug administration and start of reaction/event

User Guidance:

The major uses of intervals are to cover circumstances where both the dates are known but the interval is very short (e.g., minutes, such as in anaphylaxis), and when only imprecise dates are known but more information concerning the interval is known. Dates if available should always be transmitted in the appropriate items rather than intervals.

When there is more than one reaction/event and more than one suspect drug there is a matrix of intervals between the exposures and reactions/events. B.2.i.7 captures the interval between each reaction/event and one suspect drug. B.4.k.13 captures the interval between each suspect drug and one reaction/event. The sender should select the drug and reaction/event based on information available and/or the reporter's judgment.

NOTE CONCERNING TRANSMISSION:

THE FORMAT FOR INTERVALS IS DEFINED IN THE TRANSMISSION STANDARD .

B.4.k.13.1 Time interval between beginning of drug administration and start of reaction/event

B.4.k.13.2 Time interval between last dose of drug and start of reaction/event

B.4.k.14 Date of last administration

User Guidance:

For ongoing drug administration after the onset of the reaction/event leave this item blank and use Action(s) taken with drug (B.4.k.16).

B.4.k.15 Duration of drug administration

User Guidance:

This item is used if exact dates of drug administration are not available at the time of the report, but there is information concerning the duration of drug administration. The information requested is the overall duration of drug administration and covers intermittent administration.

NOTE CONCERNING TRANSMISSION:

THE FORMAT IS DEFINED IN THE TRANSMISSION STANDARD .

B.4.k.16 Action(s) taken with drug

- ***Drug withdrawn***
- ***Dose reduced***
- ***Dose increased***
- ***Dose not changed***
- ***Unknown***
- ***Not applicable***

User Guidance:

These data, taken together with the outcome of the reaction (B.2.i.8), provide the information concerning dechallenge. "Not applicable" is used in circumstances such as if the patient died or the treatment had been completed prior to reaction/event.

B.4.k.17 Effect of rechallenge (or re-exposure), for suspect drug(s) only

B.4.k.17.1 Did reaction recur on readministration?

- ***yes/no/unknown***

User Guidance:

Unknown indicates that a rechallenge was done but it is not known if the event recurred. This segment is not to be completed if it is unknown whether a rechallenge was done.

B.4.k.17.2 If yes to item B.4.k.17.1, which reaction(s)/event(s) recurred?

NOTE CONCERNING TRANSMISSION:

CONTROLLED VOCABULARY TO BE USED WHEN FULLY IMPLEMENTED .

B.4.k.18 Relatedness of drug to reaction(s)/event(s) (repeat B.4.k.18.1 through B.4.k.18.4 as necessary)

User Guidance:

This section provides the means to transmit the degree of suspected relatedness of each drug to the reaction(s)/event(s). The repeating items could also be used to provide the assessment of relatedness by different sources or methods of assessment. For the purpose of reporting, there is a conventional implied suspected causality for spontaneous reports. It is recognized that information concerning the relatedness, especially for spontaneous reports, is often subjective and may not be available

NOTE CONCERNING TRANSMISSION:

FOR SUBSECTION B.4.K.18.1 THE CONTROLLED VOCABULARY, WHEN FULLY IMPLEMENTED, SHOULD BE USED. FOR SUBSECTIONS B.4.K.18.2 THROUGH B.4.K.18.4 ALPHA/NUMERIC DATA WITH UNCONTROLLED VOCABULARY SHOULD BE USED .

B.4.k.18.1 Reaction assessed

User Guidance:

Generally the reaction assessed is the most important or the most serious.

B.4.k.18.2 Source of assessment

User Guidance:

e.g., initial reporter, investigator, regulatory agency, company.

B.4.k.18.3 Method of assessment

User Guidance:

E.g., global introspection, algorithm, Bayesian calculation.

B.4.k.18.4 Result

B.4.k.19 Additional inf ormation on drug

User Guidance:

Use to specify any additional information pertinent to the case that is not covered by above sections. (e.g., beyond expiration date, batch and lot tested and found to be within specifications).

B.5 NARRATIVE CASE SUMMARY AND FURTHER INFORMATION

B.5.1 Case narrative including clinical course, therapeutic measures, outcome and additional relevant information.

User Guidance:

Focused, factual and clear description of the case.

NOTE CONCERNING TRANSMISSION:

FREE TEXT

B.5.2 Reporter's comments

User Guidance:

Use for including the reporter's comments on the diagnosis, causality assessment or other issues considered relevant.

B.5.3 Sender's diagnosis/syndrome and/or reclassification of reaction/event

User Guidance:

This section provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis and the reasoning would be included in section B.5.4.

NOTE CONCERNING TRANSMISSION:

UNCONTROLLED VOCABULARY UNTIL THE CONTROLLED VOCABULARY IS FULLY IMPLEMENTED.

B.5.4 Sender's comments

User Guidance:

This section provides information concerning the sender's assessment of the case and may be used to describe disagreement with, and/or alternatives to, the diagnoses given by the initial reporter.

NOTE CONCERNING TRANSMISSION:

FREE TEXT

3. GLOSSARY

Parent-child/fetus report

Report in which the administration of medicines to a parent results in a suspected reaction/event in a child/fetus.

Receiver

The intended recipient of the transmission.

Reporter

Reporter is the primary source of the information, i.e., a person who initially reports the facts. This should be distinguished from the sender of the message, though the reporter could also be a sender.

Sender

The person or entity creating the message for transmission. Although the reporter and sender may be the same person, the function of the sender should not to be confused with that of the reporter.

ATTACHMENT 1

Unit List

Mass	
kg	kilogram(s)
g	gram(s)
mg	milligram(s)
ìg	microgram(s)
ng	nanogram(s)
pg	picogram(s)
mg/kg	milligram(s)/kilogram
ìg/kg	microgram(s)/kilogram
mg/m2	milligram(s)/sq. meter
ìg/ m2	microgram(s)/ sq. meter

Volume	
l	litre(s)
ml	millilitre(s)
ìl	microlitre(s)

Radioactivity	
Bq	becquerel(s)
GBq	gigabecquerel(s)
MBq	megabecquerel(s)
Kbq	kilobecquerel(s)
Ci	curie(s)
mCi	millicurie(s)
ìCi	microcurie(s)
nCi	nanocurie(s)

Other	
mol	mole(s)
mmol	millimole(s)
ìmol	micromole(s)
iu	international unit(s)
kiu	iu(1000s)
Miu	iu(1,000,000s)
iu/kg	iu/kilogram
mEq	milliequivalent(s)
%	percent
gtt	drop(s)
DF	dosage form

User Guidance:
This is the suggested list of units. When having other measure units, transformation is recommended if possible. Otherwise use the free text field.

Definition of Interval List

Minutes	Months
Hours	Years
Days	Cyclical
Weeks	As necessary
	Total

ATTACHMENT 2

Route of Administration List

Auricular (otic)
Buccal
Cutaneous
Dental
Endocervical
Endosinusial
Endotracheal
Epidural
Extra-amniotic
Hemodialysis
Intra corpus cavernosum
Intra-amniotic
Intra-arterial
Intra-articular
Intra-uterine
Intracardiac
Intracavernous
Intracerebral
Intracervical
Intracisternal
Intracorneal
Intracoronary
Intradermal
Intradiscal (intraspinal)
Intrahepatic
Intralesional
Intralymphatic
Intramedullar (bone marrow)
Intrameningeal
Intramuscular
Intraocular
Intrapericardial
Intraperitoneal
Intrapleural
Intrasynovial
Intratumor
Intrathecal
Intrathoracic
Intratracheal
Intravenous bolus
Intravenous drip
Intravenous (not otherwise specified)
Intravesical
Iontophoresis
Nasal
Occlusive dressing technique
Ophthalmic
Oral
Oropharingeal
Other
Parenteral
Periarticular
Perineural
Rectal
Respiratory (inhalation)
Retrobulbar
Subconjunctival
Subcutaneous
Subdermal
Sublingual
Topical
Transdermal
Transmammary
Transplacental
Unknown
Urethral
Vaginal